primary-amine oxidase 1.4.3.21

1 Nomenclature

EC number
1.4.3.21

Systematic name
primary-amine:oxygen oxidoreductase (deaminating)

Recommended name
primary-amine oxidase

Synonyms
AGAO <11> [14,15,16,32,33]
AOC2 <24> [59]
AOC3 <2,18> (<2> the major SSAO form expressed in mouse adipocytes is encoded by the AOC_3 gene [42]) [42,59]
BAO <20> [21]
BPAO <7> [13]
BSAO <7> [25]
CAO <9,11> [32,60]
Copper amine oxidase <1,3,9,11> [32,33,37,54,60]
Cu/TPQ amine oxidase <12,15,17,23> [22]
CuAO <1> [37]
ECAO <3> [11]
GPAO <23> [22]
HPAO <10,22> [17,21]
Hansenula polymorpha amine oxidase <22> [21]
LSAO <12> [22]
MAO-N <8> [55,61]
OVAO <15> [22]
PSAO <17,21> [21,22]
RAO <24> [59]
SSAO <2,4,5,7,13,18,19,24> [20,23,24,26,27,28,29,30,34,35,36,38,39,40,41,42,43,44,45,47,48,50,51,52,53,57,58,59,62,63,65,66,67,68]
SSAO/VAP-1 <2,5> [58,62]
TPQ-containing CuAO <11> [56]
VAP-1 <2,4,5,18> [57,58,59,66,67,68]
amine oxidase, copper containing <18,24> [59]
benzylamine oxidase <20> [21]
bovine plasma amine oxidase <7> [13]
bovine serum amine oxidase <7> [25]
copper amine oxidase 1 <9> [60]

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Springer Handbook of Enzymes S8, DOI 10.1007/978-3-642-36265-1_51,

copper-containing amine oxidase <11,21> [21,56]
copper-dependent amine oxidase <5> [64]
grass pea amine oxidase <23> [22]
lentil seedling amine oxidase <12> [22]
pea seedling amine oxidase <17> [22]
quinone-containing copper amine oxidase <11> [56]
sainfoin amine oxidase <15> [22]
semicarbazide-sensitive amine oxidase <2,4,5,7,13,18,19,24> [20,24,26,29,30,31,34,35,36,38,39,40,42,43,45,47,50,52,57,58,59,62,63,65,66,67,68]
semicarbazide-sensitive amine oxidase/vascular adhesion protein-1 <5> [44]
semicarbazide-sensitive amine oxidases <2,5> [42,53]
vascular adhesion protein 1 <4,5> [66,67]
vascular adhesion protein-1 <2,4,5,18> [42,57,58,59,62,68]
Additional information <4> (<4> VAP-1 belongs to the semicarbazide-sensitive amine oxidases, SSAOs [68]) [68]

2 Source Organism

<1> *Vicia faba* [37]
<2> *Mus musculus* [23,26,27,28,42,48,58]
<3> *Escherichia coli* [11,54]
<4> *Homo sapiens* [24,26,27,28,29,34,38,43,45,48,50,57,63,65,66,68]
<5> *Rattus norvegicus* (cerebral hemodynamic modifications induce decreases in SSAO activity resulting in cell dedifferentiation and inducing dysregulation of glucose transport [47]) [27,28,31,41,44,46,47,48,51,52,53,62,64,67]
<6> *Sus scrofa* [2,3,4,5,6,7]
<7> *Bos taurus* [1,13,25,28,30,39,40]
<8> *Aspergillus niger* [55,61]
<9> *Schizosaccharomyces pombe* [60]
<10> *Pichia angusta* (isozyme C4H1-1 [19]) [8,9,10,12,17,19]
<11> *Arthrobacter globiformis* [14,15,16,18,32,33,56]
<12> *Lens culinaris* [22]
<13> *Mycobacterium sp.* [35]
<14> no activity in *Saccharomyces cerevisiae* [60]
<15> *Onobrychis viciifolia* [22]
<16> no activity in *Cyprinus carpio* [49]
<17> *Pisum sativum* (UNIPROT accession number: Q43077) [22]
<18> *Homo sapiens* (UNIPROT accession number: Q16853, isoenzyme AOC3 [59]) [36,59]
<19> *Rattus norvegicus* (UNIPROT accession number: O08590) [20]
<20> *Sus scrofa* (UNIPROT accession number: Q16853) [21]
<21> *Pisum sativum* (UNIPROT accession number: Q42432) [21]
<22> *Pichia angusta* (UNIPROT accession number: P12807) [21]
<23> *Lathyrus sativus* (UNIPROT accession number: Q6A174) [22]

<24> *Homo sapiens* (UNIPROT accession number: O75106, isoenzyme AOC2 [59]) [59]

3 Reaction and Specificity

Catalyzed reaction

$RCH_2NH_2 + H_2O + O_2 = RCHO + NH_3 + H_2O_2$ (<10> role of copper in enzyme activity [10]; <10> proposed mechanism, crystal structure [9])

Natural substrates and products

- **S** 2-phenylethylamine + H_2O + O_2 <24> (Reversibility: ?) [59]
- **P** β-phenylethanal + NH_3 + H_2O_2
- **S** aminoacetone + H_2O + O_2 <4> (Reversibility: ?) [57]
- **P** methylglyoxal + NH_3 + H_2O_2
- **S** benzylamine + H_2O + O_2 <18,24> (<24> low activity [59]) (Reversibility: ?) [59]
- **P** benzaldehyde + NH_3 + H_2O_2
- **S** ethylamine + H_2O + O_2 <9> (Reversibility: ?) [60]
- **P** acetaldehyde + NH_3 + H_2O_2
- **S** methylamine + H_2O + O_2 <4,18> (Reversibility: ?) [57,59]
- **P** formaldehyde + NH_3 + H_2O_2
- **S** phenylethyl amine + H_2O + O_2 <4> (Reversibility: ?) [63]
- **P** phenylethanal + NH_3 + H_2O_2
- **S** tryptamine + H_2O + O_2 <24> (Reversibility: ?) [59]
- **P** (1H-indol-3-yl)acetaldehyde + NH_3 + H_2O_2
- **S** tyramine + H_2O + O_2 <24> (Reversibility: ?) [59]
- **P** 4-hydroxyphenylethanal + NH_3 + H_2O_2
- **S** Additional information <2,4,7,8,18,24> (<4> physiologic role for SSAO in elastin maturation [24]; <7> Semicarbazide-sensitive amine oxidase acts as a vascular-adhesion protein, mediating the adhesion of lymphocytes to vascular endothelial cells under inflammatory conditions [39]; <4> SSAO may contribute to the vascular damage associated to Alzheimer´s disease [45]; <18> synergistic interaction between semicarbazide-sensitive amine oxidase and angiotensin-converting enzyme in diabetes. Semicarbazide-sensitive amine oxidase is involved in the following biological processes: vision, inflammatory response, biogenic amine metabolism, catecholamine metabolism, amine metabolism, cell adhesion [36]; <2> T0901317 inhibits SSAO gene expression and its activity in atherogenic apoE-/- mice. The atheroprotective effect of LXR agonist T0901317 is related to the inhibition of SSAO gene expression and its activity [23]; <8> MAO-N is a flavoenzyme that catalyses the oxidative deamination of primary amines, substrate specificity, overview [61]; <18,24> semicarbazide-sensitive amine oxidases constitute a group of copper-dependent enzymes, which oxidatively deaminate primary endo- and exogenous amines [59]; <4> the catalytic center is deeply buried within the enzyme and is accessible only through a narrow channel with a diameter of about 4.5 A. This

channel is gated by the side chain of L469 which, along with the copper-TPQ coordination, controls the catalytic activity of SSAO. While specific interactions with residues lining the surface of the accessing channel are important for substrate specificity, the flexibility of substrates also plays an important role, molecular dynamics and induced docking studies, detailed overview [65]; <4> VAP-1/SSAOs convert amines into aldehydes. SSAOs are distinct from the mammalian monoamine oxidases, MAOs, but their substrate specificities are partly overlapping [68]) (Reversibility: ?) [23,24,36,39,45,59,61,65,68]

P ?

Substrates and products

S 1,4-diamino-2-butyne + H_2O + O_2 <12,15,17,23> (<12> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) (Reversibility: ?) [22]

P ?

S 1,4-diamino-2-chloro-2-butene + H_2O + O_2 <12,15,17,23> (<12> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) (Reversibility: ?) [22]

P ?

S 1,5-diamino-2-pentyne + H_2O + O_2 <12,15,17,23> (<12> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) (Reversibility: ?) [22]

P ?

S 1,6-diamino-2,4-hexadiyne + H_2O + O_2 <12,15,17,23> (<12> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) (Reversibility: ?) [22]

P ?

S 1-(3-fluoro-4-methylphenyl)methanamine + H_2O + O_2 <2,7> (Reversibility: ?) [28]

P ? + NH_3 + H_2O_2

S 1-(4-fluorophenyl)methanamine + H_2O + O_2 <2,7> (Reversibility: ?) [28]

P ? + NH_3 + H_2O_2

S 1-aminobutane + H_2O + O_2 <7> (Reversibility: ?) [25]

P butanal + NH_3 + H_2O_2

S 1-aminoheptane + H_2O + O_2 <7> (Reversibility: ?) [25]

P heptanal + NH_3 + H_2O_2

S 1-aminohexane + H_2O + O_2 <7> (Reversibility: ?) [25]

P hexanal + NH_3 + H_2O_2

S 1-aminononane + H_2O + O_2 <7> (<7> the aliphatic chain of 1-aminononane induces a shift in the pKa-value of the product Schiff base, the hydrolysis of which appears to be a rate-determining step of the reaction [25]) (Reversibility: ?) [25]
P nonanal + NH_3 + H_2O_2
S 1-aminooctane + H_2O + O_2 <7> (Reversibility: ?) [25]
P octanal + NH_3 + H_2O_2
S 1-aminopentane + H_2O + O_2 <7> (Reversibility: ?) [25]
P pentanal + NH_3 + H_2O_2
S 1-methylhistamine + O_2 + H_2O <19> (Reversibility: ?) [20]
P ?
S 2-bromoethylamine + H_2O + O_2 <12,15,17,23> (<12> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) (Reversibility: ?) [22]
P bromoacetaldehyde + NH_3 + H_2O_2
S 2-phenylethanamine + H_2O + O_2 <2,7> (Reversibility: ?) [28]
P ? + NH_3 + H_2O_2
S 2-phenylethylamine + H_2O + O_2 <3,11,19,22,24> (Reversibility: ?) [11,14,16,18,20,21,32,59]
P 2-phenylethanal + NH_3 + H_2O_2
S 3,3-bis(aminoethyl)-1-hydroxy-2-oxo-1-triazene + H_2O + O_2 <12,15,17,23> (<12> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) (Reversibility: ?) [22]
P ?
S 3-phenylpropan-1-amine + H_2O + O_2 <2,7> (Reversibility: ?) [28]
P ? + NH_3 + H_2O_2
S 4-(aminomethyl)-N-[3-(aminomethyl)benzyl]benzamide + H_2O + O_2 <2,7> (Reversibility: ?) [28]
P ? + NH_3 + H_2O_2
S 4-aminomethylpyridine dihydrochloride + H_2O + O_2 <20,21,22> (<22> 45% substrate activity of 1 mM 4-aminomethylpyridine dihydrochloride as percentage of the activity of the best substrate (β-phenylethylamine, 1 mM) for various amine oxidases [21]; <20> 87% substrate activity of 1 mM 4-aminomethylpyridine dihydrochloride as percentage of the activity of the best substrate (benzylamine, 1 mM) for various amine oxidases [21]; <21> less than 0.1% substrate activity of 1 mM 4-aminomethylpyridine dihydrochloride as percentage of the activity of the best substrate (putrescine, 1 mM) for various amine oxidases [21]) (Reversibility: ?) [21]
P ?
S 4-phenylbutan-1-amine + H_2O + O_2 <2,7> (Reversibility: ?) [28]
P ? + NH_3 + H_2O_2
S N-[3-(aminomethyl)benzyl]-4-bromobenzamide + H_2O + O_2 <2,7> (Reversibility: ?) [28]

P ? + NH_3 + H_2O_2
S N-[3-(aminomethyl)benzyl]acetamide + H_2O + O_2 <2,7> (Reversibility: ?) [28]
P ? + NH_3 + H_2O_2
S N-[3-(aminomethyl)benzyl]benzamide + H_2O + O_2 <2,7> (Reversibility: ?) [28]
P ? + NH_3 + H_2O_2
S N-[3-(aminomethyl)benzyl]propanamide + H_2O + O_2 <2,7> (Reversibility: ?) [28]
P ? + NH_3 + H_2O_2
S N^6-(4-aminobut-2-ynyl)adenine + H_2O + O_2 <12,15,17,23> (<12> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) (Reversibility: ?) [22]
P ?
S RCH_2NH_2 + H_2O + O_2 <6,7,10> (Reversibility: ?) [1,2,3,4,5,6,7,8,9,10]
P RCHO + NH_3 + H_2O_2 <6,7,10> [1,2,3,4,5,6,7,8,9,10]
S allyl [3-(aminomethyl)benzyl]carbamate + H_2O + O_2 <2,7> (Reversibility: ?) [28]
P ? + NH_3 + H_2O_2
S aminoacetone + H_2O + O_2 <4> (Reversibility: ?) [57]
P methylglyoxal + NH_3 + H_2O_2
S benzylamine + H_2O + O_2 <2,4,5,6,7,10,11,13,18,20,24> (<24> low activity [59]; <13> best oxidized substrate [35]) (Reversibility: ?) [1,2,17,21,23,24,26,27,28,29,30,31,33,34,35,38,39,40,41,42,43,44,47,48,51,52,57,59,62,67,68]
P benzaldehyde + NH_3 + H_2O_2 <6,7> [1,2]
S benzylamine + O_2 + H_2O <19> (Reversibility: ?) [20]
P benzaldehyde + NH_3 + H_2O_2
S ethylamine + H_2O + O_2 <9,10> (Reversibility: ?) [17,60]
P acetaldehyde + NH_3 + H_2O_2
S hexakis(benzylammonium) decavanadate (V) dihydrate + H_2O + O_2 <2,4,5> (Reversibility: ?) [27]
P ?
S histamine + H_2O + O_2 <13> (Reversibility: ?) [35]
P 4-imidazolylethanal + NH_3 + H_2O_2
S methyl 1-(2-methoxyethyl)-3-(trifluoroacetyl)-1H-indole-4-carboxylate + H_2O + O_2 <4> (Reversibility: ?) [65]
P ?
S methylamine + H_2O + O_2 <4,5,10,18> (Reversibility: ?) [10,12,17,19,46,57,59]
P formaldehyde + NH_3 + H_2O_2
S phenylethyl amine + H_2O + O_2 <4> (Reversibility: ?) [63]
P phenylethanal + NH_3 + H_2O_2
S putrescine + H_2O + O_2 <21> (Reversibility: ?) [21]
P ?

S pyrrolidine + 2,4,5-trihydroxyphenylalanine quinone + H_2O + O_2 <7> (Reversibility: ?) [13]
P ? + H_2O_2 + NH_3
S serotonin + O_2 + H_2O <19> (Reversibility: ?) [20]
P (5-hydroxy-1H-indol-3yl)acetaldehyde + NH_3 + H_2O_2
S tryptamine + H_2O + O_2 <12,15,17,23> (<12> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) (Reversibility: ?) [22]
P 1H-indol-3-ylacetaldehyde + NH_3 + H_2O_2
S tryptamine + H_2O + O_2 <24> (<24> high activity [59]) (Reversibility: ?) [59]
P (1H-indol-3-yl)acetaldehyde + NH_3 + H_2O_2
S tyramine + H_2O + O_2 <12> (<12> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) (Reversibility: ?) [22]
P ?
S tyramine + H_2O + O_2 <5,11,13,15,17,23,24> (<24> high activity [59]; <11> quantum mechanical hydrogen tunneling can be enhanced by an enzyme protein scaffold including the catalytic base that directly mediates the hydrogen transfer [15]) (Reversibility: ?) [15,22,35,51,53,59,62]
P 4-hydroxyphenylethanal + NH_3 + H_2O_2
S tyramine + O_2 + H_2O <19> (Reversibility: ?) [20]
P 4-hydroxyphenylethanal + NH_3 + H_2O_2
S Additional information <2,3,4,5,7,8,9,12,18,24> (<4> physiologic role for SSAO in elastin maturation [24]; <7> Semicarbazide-sensitive amine oxidase acts as a vascular-adhesion protein, mediating the adhesion of lymphocytes to vascular endothelial cells under inflammatory conditions [39]; <4> SSAO may contribute to the vascular damage associated to Alzheimer´s disease [45]; <18> synergistic interaction between semicarbazide-sensitive amine oxidase and angiotensin-converting enzyme in diabetes. Semicarbazide-sensitive amine oxidase is involved in the following biological processes: vision, inflammatory response, biogenic amine metabolism, catecholamine metabolism, amine metabolism, cell adhesion [36]; <2> T0901317 inhibits SSAO gene expression and its activity in atherogenic apoE-/- mice. The atheroprotective effect of LXR agonist T0901317 is related to the inhibition of SSAO gene expression and its activity [23]; <12> alkylamines 2-bromoethylamine and 2-chloroethylamine, and the short diamine 1,2-diaminoethane are both poor substrates and irreversible inactivators of LSAO [22]; <8> MAO-N is a flavoenzyme that catalyses the oxidative deamination of primary amines, substrate specificity, overview [61]; <18,24> semicarbazide-sensitive amine oxidases constitute a group of copper-dependent enzymes, which oxidatively deaminate primary endo- and exogenous amines [59]; <24> AOC2 is an enzymatically active cell surface SSAO with distinct substrate specificity, the

preferred in vitro substrates of AOC2 are 2-phenylethylamine, tryptamine and *p*-tyramine, cf. EC 1.4.3.4, instead of methylamine and benzylamine, the favored substrates of AOC3. Substrate docking, molecular modeling and comparison of AOC2 and AOC3, overview. No activity of AOC2 with methylamine, polyamine spermidine, or histamine [59]; <8> MAO-N is an FAD-dependent enzyme that catalyses the conversion of terminal amines to their corresponding aldehyde [55]; <18> substrate docking, molecular modeling and comparison of AOC2 and AOC3, overview. No activity of AOC3 with polyamine spermidine or histamine [59]; <3> the catalytic reaction proceeds via two half-reactions; the aldehyde product is released at the end of the reductive half-reaction before reduction of molecular oxygen in the oxidative half-reaction. Mechanism of molecular oxygen entry into the buried active site of the copper amine oxidase, the N-terminal domain does not affect oxygen entry, overview. The protein-derived cofactor TPQ and the off-metal O_2-binding site are located in the vicinity of a conserved active-site Met699 [54]; <9> three histidine residues within the C-terminal region of Cao1 that are necessary for amine oxidase activity [60]; <4> the catalytic center is deeply buried within the enzyme and is accessible only through a narrow channel with a diameter of about 4.5 A. This channel is gated by the side chain of L469 which, along with the copper-TPQ coordination, controls the catalytic activity of SSAO. While specific interactions with residues lining the surface of the accessing channel are important for substrate specificity, the flexibility of substrates also plays an important role, molecular dynamics and induced docking studies, detailed overview [65]; <4> VAP-1/SSAOs convert amines into aldehydes. SSAOs are distinct from the mammalian monoamine oxidases, MAOs, but their substrate specificities are partly overlapping [68]; <5> docking of substrates to the enzyme, the enzyme shows electrostatic control of the docking process, overview. The active site contains two negatively charged amino acid residues which seem to interact with positively charged groups of the substrate molecules [64]; <4> no activity with dimethylamide substituted indole 3-((4-[5-(aminomethyl)-2-fluorophenyl]piperidin-1-yl)carbonyl)-1-(2-methoxyethyl)-N,N-dimethyl-1H-indole-4-carboxamide [65]) (Reversibility: ?) [22,23,24,36,39,45,54,55,59,60,61,64,65,68]

P ?

Inhibitors

(1R,2S)-2-(1-methylhydrazino)-1-phenylbutan-1-ol hydrogen fumarate <4> [68]
(1R,2S)-2-(1-methylhydrazino)-1-phenylpentan-1-ol hydrogen fumarate <4> [68]
(1R,2S)-2-(1-methylhydrazino)-1-phenylpropan-1-ol hydrochloride <4> [68]
(2-methylprop-2-en-1-yl)hydrazine <7> [28]
(2-phenylprop-2-en-1-yl)hydrazine <5,7> [28]
(2E)-3-chloroprop-2-en-1-amine <7> [28]
(2Z)-3-chloroprop-2-en-1-amine <7> [28]

(Z)-3-fluoro-2-(4-methoxybenzyl)allylamine hydrochloride <2,4,5> (<2,4,5> i.e. LJP 1586. Potent, specific, and orally available inhibitor of SSAO activity is an effective anti-inflammatory compound in vivo [48]) [48]
1,2-diaminoethane <12> [22]
1,4-diamino-2-butyne <12,15,17,23> (<12,15,17,23> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) [22]
1,4-diamino-2-chloro-2-butene <12,15,17,23> (<12,15,17,23> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) [22]
1,4-phenanthroline <6,7> (<7> 0.0075 mM, 41% inhibition [1]; <6> 0.33 mM, 65% inhibition [2]) [1,2]
1,5-diamino-2-pentyne <12,15,17,23> (<12,15,17,23> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) [22]
1,6-diamino-2,4-hexadiyne <12,15,17,23> (<12,15,17,23> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) [22]
1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-(1-methylhydrazino)-ethanol hydrogen maleate <4> [68]
1-(2,5-dihydro-1H-pyrrol-3-yl)isoquinoline <7> [28]
1-(2-(3-chlorophenyl)-2-methoxyethyl)-1-methylhydrazine hydrogen fumarate <4> [68]
1-(2-chlorophenyl)-2-(1-methylhydrazino)ethanol hydrogen fumarate <4> [68]
1-(2-phenylpropyl)hydrazine hydrogen fumarate <4> [68]
1-(3,5-diethoxypyridin-4-yl)methanamine dihydrochloride <20,21,22> [21]
1-(3-methoxyphenyl)-2-(1-methylhydrazino)ethanol hydrogen fumarate <4> [68]
1-(4-methoxyphenyl)-2-(1-methylhydrazino)ethanol hydrogen fumarate <4> [68]
1-(4-chlorophenyl)-2-(1-methylhydrazino)ethanol <4> [68]
1-(4-fluorophenyl)-2-(1-methylhydrazino)ethanol hydrogen maleate <4> [68]
1-(isoquinolin-1-ylcarbonyl)pyrrolidine-2-carboxamide <4> [28]
1-[2-(2,3,4-trimethoxyphenyl)ethyl]-1-methylhydrazine hydrochloride <4> [68]
1-[2-(2,5-dimethoxyphenyl)ethyl]-1-methylhydrazine hydrogen maleate <4> [68]
1-[2-(2-chlorophenyl)ethyl]-1-methylhydrazine hydrochloride <4> [68]
1-[2-(2-fluorophenyl)ethyl]-1-methylhydrazine hydrochloride <4> [68]
1-[2-(2-methoxyphenyl)ethyl]-1-methylhydrazine hydrogen maleate <4> [68]
1-[2-(3,4,5-trimethoxyphenyl)ethyl]-1-methylhydrazine hydrogen maleate <4> [68]
1-[2-(3,4-dimethoxyphenyl)ethyl]-1-methylhydrazine hydrochloride <4> [68]

1-[2-(3-chlorophenyl)ethyl]-1-methylhydrazine hydrochloride <4> [68]
1-[2-(3-fluorophenyl)-2-methoxyethyl]-1-methylhydrazine hydrogen fumarate <4> [68]
1-[2-(3-methoxyphenyl)ethyl]-1-methylhydrazine hydrogen maleate <4> [68]
1-[2-(4-chlorophenyl)-2-methoxyethyl]-1-methylhydrazine hydrogen maleate <4> [68]
1-[2-(4-chlorophenyl)ethyl]-1-methylhydrazine hydrochloride <4> [68]
1-[2-(4-fluorophenyl)-2-methoxyethyl]-1-methylhydrazine hydrogen fumarate <4> [68]
1-[2-(4-fluorophenyl)ethyl]-1-methylhydrazine hydrogen maleate <4> [68]
1-[2-(4-fluorophenyl)prop-2-en-1-yl]-2-methylhydrazine <5> [28]
1-[2-(4-methoxyphenyl)ethyl]-1-methylhydrazine hydrogen maleate <4> [68]
1-[2-benzyloxy-2-(4-methoxyphenyl)ethyl]-1-methylhydrazine hydrogen fumarate <4> [68]
1-[2-methoxy-1-(3-tolyl)ethyl]-1-methylhydrazine hydrogen fumarate <4> [68]
1-[2-methoxy-1-(4-methoxyphenyl)ethyl]-1-methylhydrazine hydrogen fumarate <4> [68]
1-[2-methoxy-2-(1-naphthyl)ethyl]-1-methylhydrazine hydrogen fumarate <4> [68]
1-[2-methoxy-2-(2,3,4-trimethoxyphenyl)ethyl]-1-methylhydrazine hydrogen fumarate <4> [68]
1-[2-methoxy-2-(2-naphthyl)ethyl]-1-methylhydrazine hydrogen maleate <4> [68]
1-[2-methoxy-2-(3-methoxyphenyl)ethyl]-1-methylhydrazine hydrogen fumarate <4> [68]
1-[3,5-bis(ethylsulfanyl)pyridin-4-yl]methanamine dihydrochloride <20> [21]
1-[3,5-bis(tert-butylsulfanyl)pyridin-4-yl]methanamine dihydrochloride <20> [21]
1-[3-(benzyloxy)-5-ethoxypyridin-4-yl]methanamine dihydrochloride <20> [21]
1-benzyl-1-methylhydrazine hydrogen maleate <4> [68]
1-ethyl-1-(2-phenylethyl)hydrazine hydrogen maleate <4> [68]
1-ethyl-1-[2-(3,4,5-trimethoxyphenyl)ethyl]hydrazine hydrochloride <4> [68]
1-ethyl-1-[2-(4-methoxyphenyl)ethyl]hydrazine hydrochloride <4> [68]
1-ethyl-2-[2-(4-fluorophenyl)prop-2-en-1-yl]hydrazine <5> [28]
1-isobutyl-1-(2-phenylethyl)hydrazine hydrogen maleate <4> [68]
1-isobutyl-1-[2-(4-methoxyphenyl)ethyl]hydrazine hydrogen maleate <4> [68]
1-methyl-1-(2-phenylethyl)hydrazine hydrochloride <4> [68]
1-methyl-1-(2-phenylpropyl)hydrazine hydrogen fumarate <4> [68]
1-methyl-1-(3-phenylpropyl)hydrazine hydrogen maleate <4> [68]
2,2-dimethyl-2-(1'-methylhydrazino)-1-phenylethanol hydrogen fumarate <4> [68]
2-(1'-methylhydrazino)-1-(2,3,4-trimethoxyphenyl)ethanol hydrogen fumarate <4> [68]
2-(1-isobutylhydrazino)-1-phenylethanol hydrogen fumarate <4> [68]
2-(1-methylhydrazino)-1-(2-naphthyl)ethanol hydrogen maleate <4> [68]

2-(1-methylhydrazino)-1-phenylethanol hydrogen maleate hemiethanolate <4> [68]
2-(2,5-dihydro-1H-pyrrol-3-yl)pyridine <7> [28]
2-(4-[2-[2-(acetylamino)-2,3-dihydro-1,3-thiazol-4-yl]ethyl]phenyl)-N-[amino(imino)methyl]acetamide <4> [28]
2-(4-methoxyphenyl)-1-(1'-methylhydrazino)-2-propanol hydrogen maleate <4> [68]
2-([[4-(1,1-dimethylpropyl)phenyl]sulfonyl]amino)-N,3-dihydroxybutanamide <4> [28]
2-(aminooxy)-1-(3,4-dimethoxyphenyl)ethanol <7> [28]
2-(aminooxy)-1-phenylethanol <7> [28]
2-bromoethylamine <12,15,17,23> (<12,15,17,23> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) [22]
2-phenylethylamine <24> (<24> substrate inhibition [59]) [59]
2-[(biphenyl-4-ylacetyl)amino]pentanedioic acid <4> [28]
2-amino-N-[2-fluoro-3-(trifluoromethyl)benzyl]acetamide <5> [28]
2-amino-N-[2-fluoro-5-(trifluoromethyl)benzyl]acetamide <5> [28]
2-amino-N-[3-fluoro-5-(trifluoromethyl)benzyl]acetamide <5> [28]
2-amino-N-[4-fluoro-3-(trifluoromethyl)benzyl]acetamide <5> [28]
2-chloroethylamine <12> [22]
2-ethylaminobenzylamine dihydrochloride <20,21,22> [21]
2-hydrazino-1-(3-methoxyphenyl)ethanol hydrogen maleate <4> [68]
2-hydrazino-1-(4-methoxyphenyl)ethanol hydrogen maleate <4> [68]
2-hydrazino-1-phenylethanol hydrogen maleate <4> [68]
2-methylaminobenzylamine dihydrochloride <20,21,22> [21]
3,3'-[[4-(aminomethyl)pyridine-3,5-diyl]bis(oxy)]dipropan-1-ol dihydrochloride <20> [21]
3,3-bis(aminoethyl)-1-hydroxy-2-oxo-1-triazene <12,15,17,23> (<12,15,17,23> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) [22]
3-(1-piperidinyl)-4-aminomethylpyridine dihydrochloride hemihydrate <20,22> [21]
3-(2,5-dihydro-1H-pyrrol-3-yl)pyridine <7> [28]
3-(2-naphthyl)-3-pyrroline <7> (<7> 0.2 mM, inactivation of BPAO by 3-aryl-3-pyrrolines [13]) [13]
3-(4-methoxy-3-nitrophenyl)-3-pyrroline <7> (<7> 0.015 mM, inactivation of BPAO by 3-aryl-3-pyrrolines [13]) [13]
3-(4-methoxyphenyl)-2,5-dihydro-1H-pyrrole hydrochloride <7> (<7> 0.4 mM, inactivation of BPAO by 3-aryl-3-pyrrolines [13]) [13]
3-(4-methoxyphenyl)-N-methyl-5-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide <5> [28,41]
3-Pyrroline <7> [13]
3-[(1-methylethyl)amino]-4-aminomethylpyridine dihydrochloride <20,22> [21]

3-[2-(3-methoxyphenyl)ethyl]-2,5-dihydro-1H-pyrrole <5> [28]
3-amino-4-aminomethylpyridine dihydrochloride <20> [21]
3-biphenyl-4-yl-2,5-dihydro-1H-pyrrole hydrochloride <7> (<7> 0.1 mM, inactivation of BPAO by 3-aryl-3-pyrrolines [13]) [13]
3-bromoprop-2-yn-1-amine <7> [28]
3-cycloheptylamino-4-aminomethylpyridine dihydrochloride monohydrate <20,21,22> [21]
3-cyclohexylamino-4-aminomethylpyridine dihydrochloride monohydrate <20,22> [21]
3-cyclohexylmethylamino-4-aminomethylpyridine dihydrochloride monohydrate <20,21,22> [21]
3-cyclopentylamino-4-aminomethylpyridine dihydrochloride hemihydrate <20,22> [21]
3-cyclopropylamino-4-aminomethylpyridine dihydrochloride sesquihydrate <20,22> [21]
3-ethylamino-4-aminomethylpyridine dihydrochloride <20,21,22> [21]
3-methylamino-4-aminomethylpyridine dihydrochloride <20,21,22> [21]
3-naphthalen-1-yl-2,5-dihydro-1H-pyrrole hydrochloride <7> (<7> 0.4 mM, inactivation of BPAO by 3-aryl-3-pyrrolines [13]) [13]
3-phenyl-3-pyrroline <7> (<7> 0.4 mM, inactivation of BPAO by 3-aryl-3-pyrrolines [13]) [13]
4,4'-[[4-(aminomethyl)pyridine-3,5-diyl]bis(oxy)]dibutan-1-ol dihydrochloride <20> [21]
4-(2,5-dihydro-1H-pyrrol-3-yl)-N,N-dimethylaniline hydrochloride <7> (<7> 0.4 mM, inactivation of BPAO by 3-aryl-3-pyrrolines [13]) [13]
4-(2-naphthyloxy)but-2-yn-1-amine <7> [28]
4-(4-methoxyphenoxy)but-2-yn-1-amine <7> [28]
4-(4-methylphenoxy)but-2-yn-1-amine <7> [28]
4-(4-nitrophenoxy)but-2-yn-1-amine <7> [28]
4-(aminomethyl)-2-benzyl-5-(ethylamino)pyridazin-3(2H)-one <4> (<4> below 10% inhibition at 0.5 mM [66]) [66]
4-(aminomethyl)-2-methyl-5-(morpholin-4-yl)pyridazin-3(2H)-one <4> (<4> 93% inhibition at 0.5 mM [66]) [66]
4-(aminomethyl)-2-methyl-5-(pyrrolidin-1-yl)pyridazin-3(2H)-one <4> (<4> below 10% inhibition at 0.5 mM [66]) [66]
4-(aminomethyl)-5-(ethylamino)-2-methylpyridazin-3(2H)-one <4> (<4> 13% inhibition at 0.5 mM [66]) [66]
4-(aminomethyl)-N,N-diethylpyridazine-3,5-diamine <4> (<4> over 99% inhibition at 0.5 mM [66]) [66]
4-(aminomethyl)-N,N'-bis(1-methylethyl)pyridine-3,5-diamine dihydrochloride <20> [21]
4-(aminomethyl)-N,N'-dibutylpyridine-3,5-diamine dihydrochloride <20> [21]
4-(aminomethyl)-N,N'-diethylpyridazine-3,5-diamine <4> [66]
4-(aminomethyl)-N,N'-diethylpyridine-3,5-diamine dihydrochloride <20,21,22> [21]
4-(aminomethyl)-N,N'-dimethylpyridine-3,5-diamine dihydrochloride <20,21,22> [21]

4-(aminomethyl)-N-butylpyridazin-3-amine <4> (<4> 27% inhibition at 0.5 mM [66]) [66]
4-(aminomethyl)-N-ethylpyridazin-3-amine <4> (<4> 29% inhibition at 0.5 mM [66]) [66]
4-(aminomethyl)-N-methylpyridazin-3-amine <4> (<4> 47% inhibition at 0.5 mM [66]) [66]
4-(aminomethyl)-N-methylpyridine-3,5-diamine dihydrochloride <20> [21]
4-(aminomethyl)-N-propylpyridazin-3-amine <4> (<4> 44% inhibition at 0.5 mM [66]) [66]
4-amino-3-hydroxy-N-(3-phenylpropyl)benzamide <4> [28]
4-aminobut-2-ynenitrile <7> [28]
4-bromo-N-[2-(hydroxyamino)-2-oxoethyl]benzamide <4> [28]
4-phenoxybut-2-yn-1-amine <7> [28]
5-amino-2-hydroxy-N-(3-phenylpropyl)benzamide <4> [28]
8-hydroxyquinoline <7> (<7> 0.0075 mM, 27% inhibition [1]) [1]
D-galactosamine <7> [40]
KCl <13> (<13> 100 mM, 88% inhibition of dimeric and tetrameric enzyme [35]) [35]
L-Lys <7> (<7> the presence of L-lysine during the oxidation of benzylamine results in time- and dose-dependent inhibition of SSAO activity, in a process that is dependent on the H_2O_2 formed during benzylamine oxidation [39]) [39]
MDL 72223 <5> [31]
N,3-dihydroxy-2-[(2-naphthylsulfonyl)amino]butanamide <4> [28]
N-[2-(hydroxyamino)-2-oxoethyl]-2-(2-methyl-1H-indol-3-yl)acetamide <4> [28]
N-[4-(2-[4-[(2-amino-1H-imidazol-5-yl)methyl]phenyl]ethyl)-1,3-thiazol-2-yl]acetamide <4> [28]
N-[4-[2-(4-[[amino(imino)methyl]amino]phenyl)ethyl]-1,3-thiazol-2-yl]acetamide <4> [28]
N-[4-[2-(4-carbamimidamidophenyl)ethyl]-5-(4-sulfamoylbenzyl)-1,3-thiazol-2-yl]acetamide <4> [28]
N-allyl-3-(4-methoxyphenyl)-5-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide <5> [28,41]
N-ethyl-3-(4-methoxyphenyl)-5-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide <5> [28,41]
N^6-(4-aminobut-2-ynyl)adenine <12,15,17,23> (<12,15,17,23> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) [22]
NaCl <13> (<13> 100 mM, 88% inhibition of dimeric and tetrameric enzyme [35]) [35]
NaN_3 <6> (<6> uncompetitive inhibition [4]; <6> 3.3 mM, 48% inhibition [2]; <6> azide binds to Cu^{2+} ions, competitive inhibition vs. O_2, uncompetitive vs. benzylamine [6]) [2,4,6]
[(2E)-3-fluoro-2-phenylprop-2-en-1-yl]hydrazine <5> [28]
[2-(2-methylphenyl)prop-2-en-1-yl]hydrazine <5> [28]

[2-(4-chlorophenyl)prop-2-en-1-yl]hydrazine <5> [28]
[2-(4-fluorophenyl)prop-2-en-1-yl]hydrazine <5> [28]
alkylamino derivatives of 4-aminomethylpyridine, substrate-like, reversible inhibitors <22> [21]
aminoguanidine <5> (<5> strongly inhibits adipocyte semicarbazide-sensitive amine oxidase and slightly reduces fat deposition in obese Zucker rats. Aminoguanidine may be useful for treating obesity via its SSAO blocking properties [52]) [52]
benzylamine <24> (<24> substrate inhibition [59]) [59]
benzylhydrazine <11> (<11> forms adducts with the TPQ cofactor, binding structure, overview [56]) [56]
but-3-yn-1-amine <7> [28]
buta-2,3-dien-1-amine <7> [28]
cupricin <7> [1]
cuprizone <6,7> (<7> copper chelating, 0.006 mM, 98% inhibition, competitive vs. benzylamine [1]; <6> competitive binding to enzyme copper is suggested [4]) [1,4,7]
cyanide <6,7> (<7> 0.1 mM, 76% inhibition [1]; <6> uncompetitive vs. benzylamine, non-competititve vs. O_2 [6]) [1,6]
diethyldithiocarbamate <6> (<6> no inhibition [7]; <6> 3.3 mM, 74% inhibition [2]) [2,7]
extract from Taiwanofungus camphoratus <2,4> [26]
geraniin <7> (<7> competitive inhibition. Inhibitory activities of 10.87%, 37.24%, 77.67%, and 95.77%, respectively, for 0.00066, 0.00164, 0.00328, and 0.00656 mM of geraniin [30]) [30]
hydrazines <6> [5]
hydroxylamine <5,6,18,24> (<6> 3.3 mM, 30% inhibition [2]; <5> elicits hypotension in the rat. This effect is due in part to its conversion to nitric oxide and in part to a hydralazine-like action involving SSAO inhibition [46]) [2,46,59]
isoniazid <13> (<13> 0.2 mM, 42% inhibition of dimeric enzyme, 39% inhibition of tetrameric enzyme [35]) [35]
neocuproine <6> (<6> 0.033 mM, 61% inhibition [2]) [2]
o-phenylenediamine <13> (<13> 0.2 mM, 33% inhibition of dimeric enzyme, 26% inhibition of tetrameric enzyme [35]) [35]
p-chloromercuriphenylsulfonate <6> (<6> 0.1 mM, complete inhibition of enzyme from cultured aortic smooth muscle cells [7]) [7]
phenelzine <4,5,6> (<6> 0.001 mM, complete inhibition of enzyme from cultured aortic smooth muscle cells [7]) [7,53,68]
phenylhydrazine <6> (<6> irreversible inactivation most likely due to hydrazone formation [4]) [3,4,5]
rasagiline ethanedisulfonate <8> (<8> inhibits MAO-B [55]) [55]
ruthenium(II) molecular wires <11> (<11> the enzyme is reversibly inhibited by molecular wires comprising a Ru(II) complex head group and an aromatic tail group joined by an alkane linker [33]) [33]
semicarbazide <4,5,6,13,18,19,24> (<6> 0.01 mM, complete inhibition of enzyme from cultured aortic smooth muscle cells [7]; <13> 0.2 mM, 49% inhi-

bition of dimeric enzyme, 45% inhibition of tetrameric enzyme [35]; <5> irreversible inhibitor. Pargyline + semicarbazide-induced reduction of fat deposition results from decreased food intake and from impaired MAO (EC 1.4.3.4) and SSAO-dependent lipogenic and antilipolytic actions of endogenous or alimentary amines [51]; <19> causes significant decreases in the oxidative deamination activity of four among the five substrates catalyzed by SSAO [20]) [7,20,35,38,41,51,53,59,62,63,65,66,67,68]
sodium thioglycolate <7> (<7> slight [1]) [1]
tacsimate <8> [55]
tranylcypromine <3,11> (<3> fully reversible competitive onhibitor [11]; <11> forms adducts with the TPQ cofactor, also termed (1R,2S)-rel-2-phenylcyclopropanamine, is a mixture of (1R,2S)-2-phenylcyclopropanamine and (1S,2R)-2-phenylcyclopropanamine, binding structure, overview [56]) [11,56]
tryptamine <12,15,17,23,24> (<24> substrate inhibition [59]; <12,15,17,23> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) [22,59]
tyramine <12,15,17,23> (<12,15,17,23> during the oxidation of these suicide substrates, the reversible formation of an enzyme-killer product complex occurs followed by an irreversible inactivation of the enzyme, typical of mechanism-based inactivation [22]) [22]
Additional information <4,5,7,13,19> (<13> no effect: DTT or EDTA at 1 mM, 1,4-diamino-2-butanone, sodium azide or KCN [35]; <7> 3-pyrrolines are mechanism-based inactivators of the quinone-dependent amine oxidases but only substrates of the flavin-dependent amine oxidases [13]; <19> clorgyline and deprenyl do not significantly inhibit the activities [20]; <5> no inhibition by pargyline. SSAO activity remains unchanged during starvation [62]; <4> inhibitor synthesis and screening, overview [66]; <4> synthesis and in vitro activities of a series of VAP-1 selective inhibitors, molecular dynamics simulations and docking studies, pIC50 values, overview. Movements of Met211, Ser496, and especially Leu469 can enlarge the ligand-binding pocket, allowing larger ligands than those seen in the crystal structures to bind. Three-dimensional quantitative structure-activity relationship models for VAP-1 in comparison to MAOs, overview [68]) [13,20,35,62,66,68]

Cofactors/prosthetic groups

2,4,5-trihydroxyphenylalanine quinone <3,7,9,10> (<3> enzyme contains one per monomer [11]; <9> i.e. TPQ, covalently bound cofactor, one per monomer, generated by posttranslational modification of the first conserved tyrosine residue in the consensus sequence Asn-Tyr-(Glu/Asp)-Tyr [60]) [8,11,13,60]
2,4,5-trihydroxyphenylalaninequinone <3,4,11> (<3,4> i.e. TPQ cofactor [54,57]; <11> i.e. TPQ cofactor, the cofactor is spontaneously formed by post-translational modifications of active site amino-acid residues [56]) [54,56,57]
FAD <8> (<8> dependent on [55]; <8> flavoenzyme, a hydrophobic cavity extends from the protein surface to the active site, where a noncovalently

bound FAD sits at the base of an aromatic cage, the sides of which are formed by Trp430 and Phe466, binding structure, overview [61]) [55,61]
pyridoxal 5'-phosphate <6> (<6> enzyme may contain pyridoxal phosphate [4,5]) [4,5]
topaquinone <11,12,15,17,23> (<12,15,17,23> quinone of 2,4,5-trihydroxyphenylalanine, TPQ [22]) [22,32]
trihydroxyphenylalanine quinone <4> [65]
Additional information <6,13> (<6> contains one "active-carbonyl" cofactor per dimer [3]; <13> no evidences of topaquinone cofactor involvement [35]) [3,35]

Activating compounds

Atx1-like protein <9> (<9> required for the synthesis of fully active Cao1 [60]) [60]
Additional information <5,9> (<9> active Cao1 requires Ctr4/5-mediated copper transport and the transcription factor Cuf1 [60]; <5> SSAO activity remains unchanged during starvation [62]) [60,62]

Metals, ions

Co^{2+} <6,11,18,24> (<18,24> dependent on [59]; <6> can replace Cu^{2+} in the enzyme [2]; <11> enzyme reconstituted with Co^{2+} exhibits 2.2% of the activity of the original Cu^{2+} -enzyme, K_M-values for amine substrate and dioxygen are comparable [14]; <11> besides Cu^{2+} ion, some divalent metal ions such as Co^{2+}, Ni^{2+}, and Zn^{2+} are also bound to the metal site of the apoenzyme so tightly that they are not replaced by excess Cu^{2+} ions added subsequently. Although these noncupric metal ions can not initiate topaquinone formation under the atmospheric conditions, slow spectral changes are observed in the enzyme bound with Co^{2+} or Ni^{2+} ion under the dioxygen-saturating conditions. X-ray crystallographic analysis reveals structural identity of the active sites of Co- and Ni-activated enzymes with Cu-enzyme. Co^{2+} and Ni^{2+} ions are also capable of forming topaquinone, though much less efficiently than Cu^{2+} [16]) [2,14,16,59]
Cu <10> (<10> only the copper-containing homodimer is capable of rapid reoxidation and the zinc-copper heterodimers are incapable of rapid turnover at either subunit [19]) [19]
Cu^{2+} <3,4,5,9,11,12,15,17,23> (<4,5> required [66,67,68]; <5> dependent on [64]; <3> contains one Cu^{2+} per monomer [11]; <11> copper protein. The native Cu^{2+} has essential roles such as catalyzing the electron transfer between the aminoresorcinol form of the reduced topaquinone cofactor and dioxygen, in part by providing a binding site for 1e- and 2e- reduced dioxygen species to be efficiently protonated and released and also preventing the back reaction between the product aldehyde and the aminoresorcinol form of the reduced topaquinone cofactor and dioxygen [14]; <11> besides Cu^{2+} ion, some divalent metal ions such as Co^{2+}, Ni^{2+}, and Zn^{2+} are also bound to the metal site of the apoenzyme so tightly that they are not replaced by excess Cu^{2+} ions added subsequently. Although these noncupric metal ions can not initiate topaquinone formation under the atmospheric conditions, slow spectral changes are observed in the enzyme bound with Co^{2+} or Ni^{2+} ion under

the dioxygen-saturating conditions. X-ray crystallographic analysis reveals structural identity of the active sites of Co- and Ni-activated enzymes with Cu-enzyme. Co^{2+} and Ni^{2+} ions are also capable of forming topaquinone, though much less efficiently than Cu^{2+} [16]; <9> absolutely required for catalytic activity [60]; <3> type-2 copper centre, role in the catalytic mechanism, overview [54]; <4> active site bound, coordinated by three conserved histidine residues [65]) [11,14,16,22,54,60,64,65,66,67,68]
Ni^{2+} <6,11> (<6> can replace Cu^{2+} in the enzyme [2]; <11> enzyme reconstituted with Co^{2+} exhibits 0.9% of the activity of the original Cu^{2+} -enzyme, K_M-values for amine substrate and dioxygen are comparable [14]; <11> besides Cu^{2+} ion, some divalent metal ions such as Co^{2+}, Ni^{2+}, and Zn^{2+} are also bound to the metal site of the apoenzyme so tightly that they are not replaced by excess Cu^{2+} ions added subsequently. Although these noncupric metal ions can not initiate topaquinone formation under the atmospheric conditions, slow spectral changes are observed in the enzyme bound with Co^{2+} or Ni^{2+} ion under the dioxygen-saturating conditions. X-ray crystallographic analysis reveals structural identity of the active sites of Co- and Ni-activated enzymes with Cu-enzyme. Co^{2+} and Ni^{2+} ions are also capable of forming topaquinone, though much less efficiently than Cu^{2+} [16]) [2,14,16]
Zn <10> (<10> the presence of substantial amount of zinc results in two distinctive enzyme species, designated as the fast and slow enzymes. Both forms are rapidly reduced by substrate methylamine with a rate constant of 199/s but behave differently in their oxidation rates. The fast enzyme is oxidized by dioxygen at a rate of 22.1/s, whereas the slow enzyme reacts at a rate of 0.00018/s. An investigation of the relationship between the copper content and the extent of the fast enzyme shows that only the copper-containing homodimer is capable of rapid reoxidation and the zinc-copper heterodimers are incapable of rapid turnover at either subunit [19]) [19]
Zn^{2+} <6,11> (<6> can replace Cu^{2+} in the enzyme [2]; <11> besides Cu^{2+} ion, some divalent metal ions such as Co^{2+}, Ni^{2+}, and Zn^{2+} are also bound to the metal site of the apoenzyme so tightly that they are not replaced by excess Cu^{2+} ions added subsequently [16]) [2,16]
cobalt <10> (<10> the K_m-value for O_2 of the cobalt-substituted enzyme form is approximately 70fold higher than that of the copper-containing wild-type enzyme [12]) [12]
copper <4,6,7,10,11,13,22> (<4> dependent on [57]; <10> copper depleted enzyme can be reconstituted with either Cu^{2+}, Zn^{2+}, Co^{2+}, or Ni^{2+}, 79% of activity is restored with Cu^{2+}, 19% is restored with Co^{2+}, 1.7% with Zn^{2+} or Ni^{2+} [10]; <6> study of cupric ions by magnetic-resonance and kinetic methods, native enzyme contains 2 tightly bound Cu^{2+} ions [6]; <10> 2 mol copper/mol enzyme dimer [8]; <6> contains 8 Cu^{2+} per 1200000 Da, Co^{2+}, Zn^{2+} and Ni^{2+} can replace Cu^{2+}, no effect of Mn^{2+} [2]; <6> 2 mol of Cu^{2+} per dimer [3]; <6,7,10> copper protein [1,2,4,12]; <7> 3.7 gatom of copper per mol of enzyme [1]; <7> contains cupric copper [1]; <7> copper involved in enzyme activity [1]; <13> the purified enzyme contains 2.39 mol of copper per mol of subunit [35]; <7> copper-containing amine oxidase [13]; <11>

bound by three His ligands of the active-site [56]) [1,2,3,4,6,8,10,12,13,21,32,35,56,57]
sodium bicarbonate <4> (<4> activates [34]) [34]

Turnover number (s^{-1})

0.00021 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, mutant enzyme D298A [18]) [18]
0.00612 <3> (β-phenylethylamine, <3> pH 8.0, mutant enzyme D383E [11]) [11]
0.00937 <3> (β-phenylethylamine, <3> pH 7.0, mutant enzyme D383E [11]) [11]
0.01163 <3> (β-phenylethylamine, <3> pH 5.5, mutant enzyme D383E [11]) [11]
0.012 <3> (β-phenylethylamine, <3> pH 6.0, mutant enzyme D383E [11]) [11]
0.16 <10> (ethylamine, <10> pH 7, 37°C, mutant enzyme Y305F [17]) [17]
0.63 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, Ni-activated enzyme [16]) [16]
0.92 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, Co-activated enzyme [16]) [16]
1.13 <11> (O_2, <11> pH 6.8, 30°C, Ni^{2+}-substituted enzyme [14]) [14]
1.24 <11> (O_2, <11> pH 6.8, 30°C, Co^{2+}-substituted enzyme [14]) [14]
1.3 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, Ni^{2+}-substituted enzyme [14]) [14]
1.51 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, Co^{2+}-substituted enzyme [14]) [14]
2.08 <10> (methylamine, <10> Co^{2+} reconstituted enzyme [10]) [10]
2.1 <10> (O_2, <10> Co-substituted enzyme [12]) [12]
2.12 <10> (methylamine, <10> native enzyme [10]) [10]
2.7 <12> (tryptamine) [22]
7.5 <10> (ethylamine, <10> pH 7, 37°C, mutant enzyme Y305A [17]) [17]
7.8 <10> (O_2, <10> wild-type enzyme [12]) [12]
9.6 <3> (β-phenylethylamine, <3> pH 5.5, wild-type enzyme [11]) [11]
11.45 <3> (β-phenylethylamine, <3> pH 5.75, wild-type enzyme [11]) [11]
12.8 <12> (tyramine) [22]
13.32 <3> (β-phenylethylamine, <3> pH 7.5, wild-type enzyme [11]) [11]
13.68 <3> (β-phenylethylamine, <3> pH 8.0, wild-type enzyme [11]) [11]
14.98 <3> (β-phenylethylamine, <3> pH 7.0, wild-type enzyme [11]) [11]
20 <10> (ethylamine, <10> pH 7, 37°C, wild-type enzyme [17]) [17]
20.7 <3> (β-phenylethylamine, <3> pH 6.0, wild-type enzyme [11]) [11]
20.77 <3> (β-phenylethylamine, <3> pH 6.5, wild-type enzyme [11]) [11]
75.7 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, native copper protein [14]; <11> pH 6.8, 30°C, Cu-activated enzyme [16]) [14,16]
76 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, wild-type enzyme [18]) [18]
110 <11> (O_2, <11> pH 6.8, 30°C, native copper protein [14]) [14]
188-198 <6> (benzylamine) [3]

Specific activity (U/mg)

0.00015 <19> (<19> substrate benzylamine, at low substrate concentration [20]) [20]
0.00023 <19> (<19> substrate β-phenylethylamine, at low substrate concentration [20]) [20]
0.00025 <19> (<19> substrate tyramine, at low substrate concentration [20]) [20]
0.00078 <19> (<19> substrate 1-methylhistamine, at low substrate concentration [20]) [20]
0.00108 <19> (<19> substrate tyramine, at high substrate concentration [20]) [20]
0.00136 <19> (<19> substrate β-phenylethylamine, at high substrate concentration [20]) [20]
0.00165 <19> (<19> substrate 1-methylhistamine, at high substrate concentration [20]) [20]
0.00193 <19> (<19> substrate benzylamine, at high substrate concentration [20]) [20]
0.0038 <3> (<3> mutant enzyme D383E [11]) [11]
0.00388 <19> (<19> substrate serotonin, at high substrate concentration [20]) [20]
0.00555 <5> [41]
0.0193 <10> (<10> copper depleted, reconstituted with Zn^{2+} [10]) [10]
0.0195 <10> (<10> copper depleted, reconstituted with Ni^{2+} [10]) [10]
0.0571 <10> (<10> copper depleted enzyme [10]) [10]
0.105 <6> [3]
0.213 <10> (<10> copper depleted, reconstituted with Co^{2+} [10]) [10]
0.894 <10> (<10> copper depleted, reconstituted with Cu^{2+} [10]) [10]
1.13 <10> (<10> native enzyme [10]) [10]
2.08 <6> (<6> enzyme from cultured aortic smooth muscle cells [7]) [7]
3.1 <13> (<13> tetrameric enzyme [35]) [35]
5.6 <10> (<10> recombinant enzyme, methylamine oxidation [8]) [8]
6.7 <13> (<13> dimeric enzyme [35]) [35]
11 <3> (<3> wild-type enzyme [11]) [11]
Additional information <6> (<6> 1100.0-1200.0 units/mg, 1 unit is defined as the amount of enzyme catalyzing a change of 0.001 absorbance per minute at 25°C [2]) [2]

K_m-Value (mM)

0.00088 <3> (β-phenylethylamine, <3> pH 8.0, mutant enzyme D383E [11]) [11]
0.0012 <3> (β-phenylethylamine, <3> pH 7.0, wild-type enzyme [11]) [11]
0.00128 <6> (benzylamine, <6> at pH 9.0 [2]) [2]
0.0017 <3> (β-phenylethylamine, <3> pH 7.5, wild-type enzyme [11]; <3> pH 6.5, wild-type enzyme [11]) [11]
0.0018 <3> (β-phenylethylamine, <3> pH 6.0, wild-type enzyme [11]) [11]
0.0019 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, Co^{2+}-substituted enzyme [14]) [14]

0.0021 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, mutant enzyme D298A [18]) [18]
0.0023 <3> (β-phenylethylamine, <3> pH 8.0, wild-type enzyme [11]; <3> pH 5.75, wild-type enzyme [11]) [11]
0.00247 <3> (β-phenylethylamine, <3> pH 7.0, mutant enzyme D383E [11]) [11]
0.0025 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, native copper protein [14]; <11> pH 6.8, 30°C, wild-type enzyme [18]; <11> pH 6.8, 30°C, Co-activated enzyme [16]; <11> pH 6.8, 30°C, Cu-activated enzyme [16]) [14,16,18]
0.0034 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, Ni-activated enzyme [16]) [16]
0.0038 <11> (2-phenylethylamine, <11> pH 6.8, 30°C, Ni^{2+}-substituted enzyme [14]) [14]
0.0045 <13> (benzylamine, <13> dimeric enzyme [35]) [35]
0.005 <13> (benzylamine, <13> tetrameric enzyme [35]) [35]
0.0051 <6> (benzylamine, <6> enzyme from cultured aortic smooth muscle cells, K_m decreases with increasing pH [7]) [7]
0.0078 <3> (β-phenylethylamine, <3> pH 5.5, wild-type enzyme [11]) [11]
0.00962 <3> (β-phenylethylamine, <3> pH 6.0, mutant enzyme D383E [11]) [11]
0.01 <10> (methylamine, <10> native enzyme [10]) [10]
0.0127 <5> (benzylamine, <5> 37°C [27]) [27]
0.014 <5> (hexakis(benzylammonium) decavanadate (V) dihydrate, <5> 37°C [27]) [27]
0.016 <20> (4-aminomethylpyridine dihydrochloride) [21]
0.0163 <11> (O_2, <11> pH 6.8, 30°C, Co^{2+}-substituted enzyme [14]) [14]
0.017 <10> (benzylamine, <10> benzylamine oxidase [8]) [8]
0.0174 <6> (benzylamine, <6> at pH 7.2 [2]) [2]
0.0183 <11> (O_2, <11> pH 6.8, 30°C, Ni^{2+}-substituted enzyme [14]) [14]
0.0208 <11> (O_2, <11> pH 6.8, 30°C, native copper protein [14]) [14]
0.028 <3> (β-phenylethylamine, <3> pH 5.5, mutant enzyme D383E [11]) [11]
0.056 <24> (*p*-tryptamine, <24> recombinant enzyme expressed in CHO cells [59]) [59]
0.061 <2> (benzylamine, <2> 37°C [27]) [27]
0.075-0.095 <6> (benzylamine) [3]
0.077 <24> (2-phenylethylamine, <24> recombinant enzyme expressed in CHO cells [59]) [59]
0.0865 <2> (hexakis(benzylammonium) decavanadate (V) dihydrate, <2> 37°C [27]) [27]
0.124 <20> (benzylamine) [21]
0.146 <10> (methylamine, <10> recombinant enzyme [8]) [8]
0.167 <24> (benzylamine, <24> recombinant enzyme expressed in CHO cells [59]) [59]
0.178 <24> (tyramine, <24> recombinant enzyme expressed in CHO cells [59]) [59]

0.213 <4> (hexakis(benzylammonium) decavanadate (V) dihydrate, <4> 37°C [27]) [27]
0.287 <4> (benzylamine, <4> 37°C [27]) [27]
0.5 <12> (tryptamine) [22]
0.67 <18> (methylamine, <18> recombinant enzyme expressed in CHO cells [59]) [59]
0.68 <10> (methylamine, <10> Co^{2+} reconstituted enzyme [10]) [10]
0.682 <10> (benzylamine, <10> recombinant enzyme [8]) [8]
0.71 <12> (tyramine) [22]
1 <17> (1,4-diamino-2-butyne) [22]
1.49 <7> (benzylamine) [1]
1.7 <24> (methylamine, <24> recombinant enzyme expressed in CHO cells [59]) [59]
1.94 <18> (2-phenylethylamine, <18> recombinant enzyme expressed in CHO cells [59]) [59]
Additional information <5,10,18,24> (<10> the K_m-value for O_2 of the cobalt-substituted enzyme form is approximately 70fold higher than that of the copper-containing wild-type enzyme [12]; <18,24> comparison of steady-state kinetics of enzyme expressed in CHO and HEK-293 EBNA cells, overview [59]; <5> kinetic analysis at different ionic strength and pH, overview [64]) [12,59,64]

K_i-Value (mM)

0.0007 <7> (geraniin, <7> pH 7.4, 37°C [30]) [30]
0.0054 <5> (semicarbazide, <5> 37°C, 60 min preincubation [41]) [41]
0.01 <15> (1,5-diamino-2-pentyne) [22]
0.0128 <5> (semicarbazide, <5> 37°C, no preincubation [41]) [41]
0.014 <7> (cuprizone) [1]
0.032 <24> (tryptamine, <24> recombinant enzyme expressed in CHO cells [59]) [59]
0.0374 <7> (L-Lys, <7> pH 7.2, 37°C [39]) [39]
0.042 <5> (3-(4-methoxyphenyl)-N-methyl-5-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide, <5> 60 min preincubation [41]) [41]
0.05 <23> (1,5-diamino-2-pentyne) [22]
0.054 <12> (2-bromoethylamine) [22]
0.07011 <5> (3-(4-methoxyphenyl)-N-methyl-5-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide, <5> no preincubation [41]) [41]
0.08 <24> (2-phenylethylamine, <24> recombinant enzyme expressed in CHO cells [59]) [59]
0.089 <24> (benzylamine, <24> recombinant enzyme expressed in CHO cells [59]) [59]
0.17 <5> (N-ethyl-3-(4-methoxyphenyl)-5-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide, <5> 60 min preincubation [41]) [41]
0.225 <5> (N-allyl-3-(4-methoxyphenyl)-5-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide, <5> 60 min preincubation [41]) [41]
0.23 <5> (N-ethyl-3-(4-methoxyphenyl)-5-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide, <5> no preincubation [41]) [41]

0.28 <12> (3,3-bis(aminoethyl)-1-hydroxy-2-oxo-1-triazene) [22]
0.28 <5> (N-allyl-3-(4-methoxyphenyl)-5-(1H-pyrrol-2-yl)-4,5-dihydro-1H-pyrazole-1-carbothioamide, <5> no preincubation [41]) [41]
0.32 <17> (1,4-diamino-2-butyne) [22]
0.76 <6> (cyanide, <6> vs. O_2, deduced from slope [6]) [6]
2.17 <6> (cyanide, <6> vs. benzylamine [6]) [6]
2.9 <6> (cyanide, <6> vs. O_2, deduced from intercept [6]) [6]
40 <6> (N_3^-, <6> approx. value [4]) [4]
40 <6> (azide, <6> vs. benzylamine [6]) [6]
84 <6> (azide, <6> vs. O_2 [6]) [6]

pH-Optimum

7 <13> (<13> specific activities of dimeric and tetrameric enzyme form in Tris buffer at pH 7.0 is about 6fold lower than those in phosphate buffer at same pH [35]) [35]
7.4 <4,9> (<4,9> assay at [57,60,66]) [57,60,66]
7.6 <4> (<4> assay at [68]) [68]
9 <6> (<6> 50 mM glycine, 1 mM EDTA [2]) [2]

pH-Range

5.6-10.2 <5> (<5> assay range [64]) [64]
6-10 <6> [2]
Additional information <11> [18]

Temperature optimum (°C)

37 <4,9> (<4,9> assay at [57,60,68]) [57,60,68]
40 <6> [2]

Temperature range (°C)

20-40 <6> (<6> relative activity at 20°C: 22.8%, at 40°C: 31.2% [2]) [2]

4 Enzyme Structure

Molecular weight

150000 <13> (<13> dimer, gel filtration [35]) [35]
184000 <5> (<5> non-denaturing PAGE [41]) [41]
186000 <6> (<6> sedimentation-equilibrium [6]) [6]
196000 <6> (<6> gradient PAGE [3]) [3]
300000 <13> (<13> tetramer, gel filtration [35]) [35]
1200000 <6> (<6> gel filtration [2]) [2]

Subunits

? <6> (<6> x * 130000, SDS-PAGE [7]) [7]
dimer <4,5,6,9,13,15> (<13> 2 * 75000, SDS-PAGE [35]; <6> 2 * 95000, SDS-PAGE [3]; <6> 2 * 97000, SDS-PAGE [6]; <5> 2 * 93000, SDS-PAGE after treatment with 2-mercaptoethanol [41]; <4> human SSAO is a dimeric membrane protein with a short N-terminal cytoplasmic tail, a membrane-spanning domain, and an extracellular catalytic domain. The catalytic center is deeply

buried within the enzyme and is accessible only through a narrow channel with a diameter of about 4.5 A, gated by the side chain of L469 which, along with the copper-TPQ coordination, controls the catalytic activity of SSAO, conformational changes, detailed overview [65]) [3,6,22,35,41,60,65,67]
homotetramer <8> (<8> MAO-N exists as a homotetramer with a large channel at its centre [61]) [61]
octamer <6> (<6> 8 * 146000 [2]) [2]
tetramer <8,13> (<13> 4 * 75000, SDS-PAGE [35]) [35,55]
Additional information <3,18,24> (<24> AOC2 structure homology modelling, comparison with AOC3 [59]; <18> AOC3 structure homology modelling, comparison with AOC2 [59]; <3> Escherichia coli copper amine oxidase possesses an extra N-terminal domain that lies close to one entrance to the β-sandwich in the structurally conserved β-sandwich structure [54]) [54,59]

Posttranslational modification

flavoprotein <8> [61]
glycoprotein <6> (<6> heterogenity of pig plasma amine oxidase may be due to variable carbohydrate content [3]) [3]
Additional information <12,15,17,23> (<12,15,17,23> topaquinone is derived by post-translational modification of a conserved tyrosine residue in the protein chain [22]) [22]

5 Isolation/Preparation/Mutation/Application

Source/tissue

B16-F10 cell <2> [26]
HT-1080 cell <4> [26]
adipocyte <2,4,5> (<2> major SSAO form expressed in mouse adipocytes is encoded by the AOC3 gene [42]; <4> most of the SSAO found in adipose tissue originates from mature adipocytes [38]; <5> SSAO inhibition is not sufficient to impair fat deposition. However, combined monoamine oxidase (EC 1.4.3.4) inhibition and SSAO inhibition limits adiposity in non-obese as well as in obese rats [53]; <2> the major SSAO form expressed in mouse adipocytes is encoded by the AOC3 gene [42]) [38,42,52,53,57,58]
adipose tissue <2,4,5> (<4> most of the SSAO found in adipose tissue originates from mature adipocytes [38]; <2> SSAO activity is present in white adipose tissues of wild type but is absent in AOC3KO mice [42]; <5> SSAO activity regulates NO availability in white adipose tissue [31]) [27,28,31,38,42]
aorta <2,4> [34,48]
blood plasma <4,6,7> (<4> semicarbazide-sensitive amine oxidase overexpression in cerebrovascular tissue of patients with Alzheimer´s disease cerebral amyloid angiopathy correlates with high SSAO activity in plasma of severe Alzheimer´s disease patients [45]) [1,3,4,5,6,28,30,34,39,40,45]
blood serum <4,5> (<4> decreased SSAO serum activity in schizophrenic patients treated with second generation antipsychotics known to disturb glucose metabolism [29]; <4> reduced enzyme activity is found in haemodia-

lysed uremic patients before and after dialysis treatment, compared to controls. The activity is slightly lower in peritoneally dialysed, and normal in not dialysed patients. In haemodialysed patients SSAO activity is elevated compared to controls [43]; <5> treatment with benzylamine + vanadate reduces the elevated serum SSAO activity, decreases the accumulation of advanced-glycation end products and increases the bioavailability of nitric oxide in diabetic animals, similarly to insulin [44]) [29,43,44]
brain <4,24> (<4> cerebral vascular SSAO-catalysed deamination contributes to cerebral amyloid angiopathy in Alzheimer´s disease brains [50]) [50,59]
cartilage <24> [59]
cerebrovascular tissue <4> (<4> semicarbazide-sensitive amine oxidase is overexpressed in cerebrovascular tissue of patients with Alzheimer´s disease cerebral amyloid angiopathy. The enzyme colocalizes with β-amyloid deposits [45]) [45]
culture condition:benzylamine-grown cell <13> [35]
dental pulp <4> [63]
endothelial cell <2> [58]
endothelium <5> [67]
eye <4,24> [57,59]
guard cell <1> (<1> CuAO in Vicia faba guard cells is an essential enzymatic source for H_2O_2 production in absicic acid-induced stomatal closure via the degradation of putrescine [37]) [37]
heart <4,24> [57,59]
kidney <4,6,24> [2,57,59]
liver <4,5,7,24> (<5> luminal expression, immunohistochemic analysis, overview [67]) [13,57,59,64,67]
lung <4,5,18,24> [28,41,48,57,59]
ovary <24> [59]
pancreas <4,24> [57,59]
placenta <4> [57]
plasma <7> [13]
prostate gland <24> [59]
retina <18,24> [59]
seedling <12,17,21> [21,22]
serum <4,5,20> (<4> significantly elevated serum SSAO activity in diabetic patients, overview [57]) [21,57,67]
skin <24> [59]
testis <24> [59]
umbilical cord <4> [48]
vascular smooth muscle cell <4> [57]
white adipose tissue <2,5> (<5> very high activity [62]) [58,62]
Additional information <24> (<24> tissue expression pattern of AOC2, overview [59]) [59]

Localization

cell surface <5,24> (<5> of adipocytes [62]) [59,62]
extracellular <5> [67]

membrane <2,4,5,18,24> [27,34,58,59,65,67]
mitochondrion <5> [64]
peroxisome <10> [8,9]
soluble <4> [34]

Purification

<5> [41]
<6> [3,7]
<7> [1,25]
<8> (recombinant His-tagged wild-type and mutants enzymes from Escherichia coli strain Rosetta2(DE3), removal of the His tag) [55]
<8> (recombinant selenomethionine-labeled truncated mutant MAO-N-D5 from Escherichia coli strain B834(DE3) by nickel affinity chromatography) [61]
<10> [10]
<10> (native and recombinant enzyme) [8]
<11> [14,32]
<11> (recombinant enzyme expressed in Escherichia coli) [16]
<13> [35]

Crystallization

<3> (purified enzyme with xenon is used as a molecular oxygen binding-site probe, 8 mg/ml protein in 100 mM HEPES pH 7 and 1.2 M sodium citrate, vappour diffusion method, 18°C, 2 weeks, X-ray diffraction structure determination and analysis at 2.5 A resolution, modelling) [54]
<6> [2]
<8> (purified recombinant genetic variants MAO-N-3 and MAO-N-5, from 10% w/v PEG 3350, 0.2 M proline, 0.1 M HEPES, pH 7.5, or 10% w/v PEG 5000 MME, 5% v/v tacsimate, 0.1 M HEPES, pH 7.0, with no difference in diffraction quality between the crystals from the two conditions, X-ray diffraction structure determination and analysis at 2.45 A and 1.85 A resolution, respectively) [55]
<8> (purified recombinant mutants MAO-N-D3 and MAO-N-D5, and truncated selenomethionine-labeled mutant MAO-N-D5, X-ray diffraction structure determination and analysis, multiple-wavelength anomalous diffraction and molecular replacement) [61]
<10> (sitting drop, orthorhombic crystals, X-ray structure, 2.4 A) [9]
<11> (X-ray crystal structures of the Co^{2+} and Ni^{2+}-enzyme are solved at 2.0-1.8 A resolution) [14]
<11> (hanging-drop vapor diffusion method. Crystal structures of a series of Ru(II)-wire-enzyme complexes differing with respect to the length of the alkane linker) [33]
<11> (holenzyme, in which topaquinone is generated by incubation with Co^{2+} or Ni^{2+} and apoenzyme are crystallized by microdialysis method) [16]
<11> (purified recombinant C-terminal StrepII-tagged enzyme in complex with inhibitors benzylhydrazine or tranylcypromine, vapour diffusion in hanging drop method, mixing of protein solution containing about 10 mg/ml protein in 50 mM HEPES, pH 7.0, with well solution containing 1.6 M ammonium sulfate and 150 mM sodium citrate pH 7.0. $CuSO_4$, in a twofold

molar excess, 2 weeks. The crystals are then transferred to a sitting drop well solution containing 30% v/v glycerol and 2 mM benzylhydrazine dihydrochloride or 0.4 mM tranylcypromine for 30 min, X-ray diffraction structure determination and analysis at 1.65-1.86 A resolution) [56]
<11> (the X-ray crystal structure of D298K at 1.7 A resolution) [32]

Cloning

<4> (expression in CHO cells) [68]
<4> (mice overexpressing human semicarbazide-sensitive amine oxidase in smooth muscle cells. No differences in elastin quantity or lung capacity could be observed between transgenic or nontransgenic littermates. Pulse pressure is higher in transgenic mice, and aorta shows elastin fibers parallel with the aorta wall (i. e., straight fibers instead of folded compared with control mice). No difference in the response to adrenaline or sodium chloride is observed between the transgenic and control mice. The control mice have a clear decrease in blood pressure with a longer duration as a response to injection of a nitric oxide donor, sodium nitroprusside, compared with transgenic mice where only a minor response is observed. The SSAO activity in serum of control mice is elevated in response to injection of the NO donor, but not in response to a ganglion blocker) [24]
<4> (overexpression in CHO cells) [65]
<8> (expression of wild-type and mutant enzymes, expression of selenomethionine-labeled truncated mutant MAO-N-D5 in Escherichia coli strain B834(DE3)) [61]
<8> (overexpression of His-tagged wild-type and mutants enzymes in Escherichia coli strain Rosetta2(DE3)) [55]
<9> (genes cao1+ and cao2+, cDNA library screening, DNA and amino acid determination and analysis, both genes are expressed in wild-type cells, but only the expression of cao1+,not of cao2+, results in production of an active enzyme. Expression of cao1+ and cao2+ is copper-independent and is not regulated by Cuf1. Recombinant expression of GFP-tagged Cao1 in the cytosol, expression of wild-type and mutant enzymes in Saccharomyces cerevisiae) [60]
<10> [10]
<10> (expression Saccharomyces cerevisiae) [8]
<18> (AOC3, cDNA library screening, transient expression of wild-type and mutant enzymes in HEK293, HEK293-EBNA or CHO cells) [59]
<19> (expressed in COS-1 cells) [20]
<24> (AOC2, cDNA library screening, DNA and amino acid sequence determination and analysis, transient expression of wild-type enzyme in HEK293, HEK293-EBNA or CHO cells) [59]

Engineering

D298A <11> (<11> K_m-value for 2-phenylethylamine is 85% of the wild-type enzyme, k_{cat} for 2-phenylethylamine is 360000fold lower than wild-type enzyme [18]) [18]
D298K <11> (<11> in contrast to M602K and wild-type enzyme, the quinone in D298K does not react with any of the hydrazines. D298K shows no activity

toward oxidative deamination of 2-phenylethylamine. The quinone formed in D298K is trapped in a conformation that can not react with amines. D298K contains a quinone other than topaquinone [32]) [32]
D383E <3> (<3> turnover-number of mutant enzyme is reduced up to 2000fold, depending on pH-value [11]) [11]
D383N <3> (<3> catalytically inactive mutant enzyme [11]) [11]
H456A <9> (<9> site-directed mutagenesis, the active site residue mutant shows reduced activity compared to the wild-type enzyme [60]) [60]
H458A <9> (<9> site-directed mutagenesis, the active site residue mutant shows reduced activity compared to the wild-type enzyme [60]) [60]
H460A <9> (<9> site-directed mutagenesis, the active site residue mutant shows reduced activity compared to the wild-type enzyme [60]) [60]
H621A <9> (<9> site-directed mutagenesis, the mutant shows unaltered activity compared to the wild-type enzyme [60]) [60]
H627A <9> (<9> site-directed mutagenesis, the mutant shows unaltered activity compared to the wild-type enzyme [60]) [60]
M211V/Y394N/L469G <18> (<18> AOC_3 mutant [59]) [59]
M602K <11> (<11> the mutant enzyme shows 20% activity toward 2-phenylethylamine in comparison to wild-type enzyme [32]) [32]
N336S/M348K/I246M <8> (<8> gain-of-function mutant MAO-N-D3, structure analysis, overview. Of the mutations that confer the ability to catalyse the oxidation of secondary amines in MAO-N-D3, Asn336Ser reduces steric bulk behind Trp430 of the aromatic cage and Ile246Met confers greater flexibility within the substrate binding site [61]; <8> genetic variant MOA-N-3 exhibits improved activity towards a range of amine substrates compared to the wild-type enzyme, including chiral secondary amines [55]) [55,61]
N336S/M348K/I246M/T384N/D385S <8> (<8> gain-of-function mutant MAO-N-D5 is able to oxidise tertiary amines, structure analysis, overview. Of the mutations that confer the ability to catalyse the oxidation of secondary amines in MAO-N-D3, Asn336Ser reduces steric bulk behind Trp430 of the aromatic cage and Ile246Met confers greater flexibility within the substrate binding site. The two additional mutations, Thr384Asn and Asp385Ser, appear to influence the active-site environment remotely through changes in tertiary structure that perturb the side chain of Phe382, again altering the steric and electronic character of the active site near FAD [61]; <8> genetic variant MOA-N-5 shows improved activity and enantioselectivity towards a broad range of tertiary amines compared to the wild-type enzyme [55]) [55,61]
Y305A <10> (<10> mutation has moderate effects on the kinetics of catalysis (2.7fold and 8fold decrease in k_{cat} using ethylamine and benzylamine as substrates), the same mutation slows cofactor formation by about 45-fold relative to that of the wild-type enzyme. The Y305A mutant forms at least two species: primarily topaquinone at lower pH and a species with a blue-shifted absorbance at high pH [17]) [17]
Y305F <10> (<10> the rate of topaquinone formation is reduced 3fold relative to that of wild-type enzyme, 125fold decrease in k_{cat} using ethylamine as substrate [17]) [17]

Additional information <2,8> (<2> construction of AOC3-KO mice which show white adipose tissue with lower CD45 mRNA levels and fewer CD45+ leukocytes and diminished infiltration by T cells, macrophages, natural killer, and natural killer T cells, the phenotype is not rescued by human SSAO/VAP-1 expression on adipocytes under the control of aP2, overview [58]; <8> genetic variants of MAO-N produced by directed evolution possess altered substrate specificity, e.g. MAO-N-3 and MAO-N-5 [55]) [55,58]

Application

medicine <2,4,5> (<2,4,5> hexakis(benzylammonium) decavanadate (V) dihydrate acts as a prodrug of peroxovanadate insulin mimetics. SSAO oxidizes hexakis(benzylammonium) decavanadate (V) dihydrate to the same extent as it does benzylamine [27]; <4> VAP-1 might be a target for anti-inflammatory drug therapy because of its role in leukocyte adhesion to endothelium [68]) [27,68]

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